

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the applications:

Listing of Claims:

Claims 1-61 (canceled)

62. (currently amended) A protein comprising

(a) a human tumor necrosis factor (TNF)-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor (i) specifically binds human TNF tumor necrosis factor (TNF), (ii) has an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, and (iii) comprises a ~~fragment of the amino acid sequence set forth in SEQ ID NO: 4~~ LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10); and

(b) all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region;
wherein said protein specifically binds human TNF.

Claims 63-101 (canceled)

102. (currently amended) The protein of claim 62 ~~or 66~~, wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8).

103. (previously presented) The protein of claim 102, wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

104. (canceled)

105. (currently amended) The protein of claim ~~[[104]]~~ 62, wherein said human immunoglobulin IgG heavy chain is IgG₁.

106. (currently amended) A protein comprising

(a) a human tumor necrosis factor (TNF)-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor (i) specifically binds human TNF tumor necrosis factor (TNF), (ii) has an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, and (iii) comprises ~~a fragment of~~ the amino acid sequences ~~set forth in SEQ ID NO: 4~~ LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), LCAP (SEQ ID NO: 12), VFCT (SEQ ID NO: 8), NQPQAPGVEASGAGEA (SEQ ID NO: 9) and VPHLPAD (SEQ ID NO: 13),

wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8); and

(b) all of the domains of the constant region of a human IgG₁ heavy chain other than the first domain of the constant region;

wherein said protein specifically binds human TNF.

107. (currently amended) A recombinant protein encoded by a polynucleotide which comprises two nucleic acid subsequences,

(a) one of said subsequences encoding a human TNF-binding soluble fragment of an insoluble human TNF receptor protein having an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, said soluble fragment comprising a ~~fragment of~~ the amino acid sequence ~~of SEQ ID NO: 4~~ LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and

(b) the other of said subsequences encoding all of the domains of the constant region of the heavy chain of a human IgG immunoglobulin other than the first domain of said constant region,

wherein said recombinant protein specifically binds human TNF.

Claims 108 and 109 (canceled)

110. (previously presented) The protein of claim 107, wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8).

111. (previously presented) The protein of claim 110, wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

112. (canceled)

113. (currently amended) The protein of any one of claims 107, 110 or 111, wherein said human immunoglobulin heavy chain is IgG₁.

114. (currently amended) A pharmaceutical composition comprising the recombinant protein of any of claims 62, [[66,]] 107, 134 or 135 and a pharmaceutically acceptable carrier material.

Claims 115-118. (canceled)

119. (previously presented) The protein of claim 62, wherein the protein is purified.

120. (previously presented) The protein of claim 62, wherein the protein is produced by CHO cells.

121. (currently amended) The protein of claim 62, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human immunoglobulin IgG heavy chain other than the first domain of the constant region.

122. (canceled)

123. (currently amended) The protein of claim [[104]] 62, wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG

under No. DSM 5314) or by pCD4-Hy3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5523).

124. (previously presented) The protein of claim 105, wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314).

125. (previously presented) The protein of claim 106, wherein the protein is purified.

126. (previously presented) The protein of claim 106, wherein the protein is produced by CHO cells.

127. (previously presented) The protein of claim 106, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human IgG₁ heavy chain other than the first domain of the constant region.

128. (previously presented) The protein of claim 106, wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

129. (previously presented) The recombinant protein of claim 107, wherein the recombinant protein is purified.

130. (previously presented) The recombinant protein of claim 107, wherein the recombinant protein is produced by CHO cells.

131. (previously presented) The recombinant protein of claim 107, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human IgG₁ heavy chain other than the first domain of the constant region.

132. (currently amended) The protein of claim [[112]]] 107, wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or by pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

133. (previously presented) The protein of claim 113, wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by the DNA insert of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

134. (currently amended) A protein consisting of
(a) a human tumor necrosis factor (TNF)-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor (i) specifically binds human TNF, and (ii) has an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel and (iii) comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10),

wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO:12) and VFCT (SEQ ID NO:8), and

(b) all of the domains of the constant region of a human IgG₁ heavy chain other than the first domain of the constant region,

wherein the protein specifically binds human TNF, and

wherein the protein is produced by CHO cells.

135. (previously presented) The protein of claim 134, wherein the soluble fragment comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

136. (previously presented) The protein of claim 134, wherein the protein is purified.

137. (previously presented) A pharmaceutical composition comprising the recombinant protein of claim 105 and a pharmaceutically acceptable carrier material.

138. (canceled)

139. (new) A method of binding human TNF *in vivo* comprising the step of administering to a subject the pharmaceutical composition of claim 137.

140. (new) A protein comprising

(a) a human tumor necrosis factor (TNF) binding soluble fragment of the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC on _____ under accession number _____; and

(b) all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region;
wherein said protein specifically binds human TNF.

141. (new) The protein of claim 140 consisting of the soluble fragment and all the domains of the constant region of the human immunoglobulin IgG heavy chain other than the first domain of said constant region.

142. (new) The protein of claim 140
wherein the protein is expressed by a mammalian host cell.

143. (new) The protein of claim 142, wherein the mammalian host cell is a CHO cell.

144. (new) The protein of claim 142 consisting of the soluble fragment and all the domains of the constant region of the human immunoglobulin IgG heavy chain other than the first domain of said constant region.